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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,960	05/14/2007	Gabriele Multhoff	KNAUTHE-12013	7046
72960	7590		EXAMINER	
Casimir Jones, S.C. 440 Science Drive Suite 203 Madison, WI 53711			LI, RUIXIANG	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/581,960	Applicant(s) MULTHOFF, GABRIELE	
	Examiner RUIXIANG LI	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01/15/2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 18-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 18-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 June 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Restriction/Election

1. Applicant's election without traverse of Group I (claims 1-11 and 18-21) in the reply filed on 01/15/2009 is acknowledged. Applicant's election with traverse of species human colon tumor in the reply filed on 01/15/2009 is also acknowledged. The traversal is on the ground(s) that all species retain the special technical feature of possession of the common epitopes recited in claim 1. This is not found persuasive because the technical feature of possession of the common epitopes recited in claim 1 is not a special technical feature as it does not make a contribution over the prior art in view of Multhoff (WO 02/22656 A2). Multhoff teaches various tumors (page 21, the 2nd paragraph), such as the human colon carcinoma subline CX⁺, which expresses epitopes of Hsp70 on the cell surface (Example 2). Therefore, the shared technical feature does not make a contribution over the prior art

The requirement is still deemed proper and is therefore made FINAL.

2. In the preliminary amendment filed on 06/05/2009, Applicants canceled claims 12-17, 22-25, 28-30, 32, 34, and 36-39. The restriction requirement was made based upon such an amendment. In the amendment filed 01/15/2009, Applicants further canceled non-elected claims 26, 27, 31, 33, and 35. Thus, claims 1-11 and 18-21 are actually pending and currently under consideration.

Drawings

3. The drawings filed on 06/05/2006 are accepted by the Examiner.

Priority

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections—35 USC § 101

5. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 1-3, 6, and 7 are rejected under 35 U.S.C. §101 because the claimed invention is directed non-statutory subject matter.

Claims 1-3, 6, and 7, as written, do not sufficiently distinguish over an antibody that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed product and the naturally occurring product. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claim should be amended to indicate the hand of the inventor, e.g., by insertion of “isolated” or “purified”. See MPEP 2105.

Claim Rejections—35 USC § 112, 2nd paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-11 and 18-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11 are indefinite because they recite the acronym, "Hsp70", whereas claims 18-21 recite "cell surface membrane-bound heat shock protein (HSP)". First, such a term is determined arbitrarily without a definitive structure. Others in the field may isolate the same protein and give an entirely different name. Thus, claiming biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly claim what the protein is. Applicants should particularly point out and distinctly claim the Hsp70 or HSP polypeptide by claiming characteristics associated with the polypeptide, such as a sequence identifier (SEQ ID NO).

Claim Rejections—35 U.S.C. §102 (b)

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-4, 6, 7, 10, and 18-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Multhoff (WO 02/22656 A2, 21 March 2002).

Multhoff teaches a mouse monoclonal antibody, RPN1197, which binds to an extracellularly localized epitope of Hsp70 on tumor cells (Example 1; page 21, the 3rd paragraph), such as human colon carcinoma sublines CX+ (page 29, the 3rd paragraph). This antibody inhibits the cytolytic activity of NK cells against Hsp70 expressing tumor cells (page 22, last paragraph to top of page 23). Multhoff teaches the 8-mer peptide NLLGRFEL as the relevant recognition structure for the mAbRPN1197 (page 23, lines 2-5).

Since the mAb RPN1197 binds the same epitope as that of the mAb cmHsp70.1 or cmHsp70.2, the mAb RPN1197 would compete with the mAb cmHsp70.1 or cmHsp70.2 for binding to an extracellularly localized epitope of Hsp70 on human tumor cells. Since Multhoff teaches mAb RPN1197, Multhoff inherently teaches a hybridoma that produces a mAb RPN1197.

Multhoff teaches that epitope mapping analysis of mAb RPN1197 was performed using pepspot membranes with horseradish peroxidase conjugates and chemiluminescent luminol (page 28, the 2nd paragraph). Thus, Multhoff teaches mAb with a label (one functional domain), meeting the limitations 18-21.

Accordingly, the teachings of Multhoff meet the limitations of claims 1-4, 6, 7, 10, and 18-21.

Claim Rejections under 35 U.S.C. §103(a)

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Multhoff (WO 02/22656 A2, 21 March 2002), as applied to claims 1-4, 6, 7, 10, and 18-21 above, and further in view of Adair et al. (WO 91/16928 A1).

Multhoff teaches a mouse monoclonal antibody, RPN1197, which binds to an extracellularly localized epitope of Hsp70 on tumor cells, as applied to claims 1-4, 6, 7, 10, and 18-21 above. Multhoff does not explicitly teach a human, humanized, xenogenetic, or a chimeric human-murine antibody, or an antigen-binding fragment.

Adair et al. teach a humanized antibody (page 2, line 18; page 21, line 9), or an antigen-binding fragment, such as Fab and (Fab')₂ (page 2, lines 19-20; page 21, lines 22-27).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to further optimize the functions of the antibody of RPN1197 and to prepare other forms of antibodies, such as a humanized antibody or an antigen fragment as taught by Adair et al. with a reasonable expectation of success. One would have been motivated to do so because an antibody fragment, such as Fab, (Fab')₂, or a single chain antibody, is highly soluble and offers therapeutic advantages in biological half life (top of page 22), whereas a humanized antibody offers a reduced antigenicity of the antibody in a human patient (i.e., HAMA response; top of page 15), as taught by Adair et al.

Claim Objection—Minor Informalities

13. Claims 2 are objected to because of the following minor informalities: (i). claim 2 recites "and/or" in line 3; (ii). claim 2 recites "wherein said tumor..." in line 1, whereas claim 1 recites "tumor cells" in line 2, which is inconsistent; (iii). claim 2 recites non-elected species. Appropriate correction is required.

Conclusion

14. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you

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have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/

Primary Examiner, Art Unit 1646

Ruixiang Li, Ph.D.

April 13, 2009